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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/148,234	09/04/1998	IOANNIS MOUTSATSOS	P-4739-US	3002
49443 7590 08/24/2007 PEARL COHEN ZEDEK LATZER, LLP 1500 BROADWAY 12TH FLOOR NEW YORK, NY 10036			EXAMINER POPA, ILEANA	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 08/24/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/148,234	<b>Applicant(s)</b> MOUTSATSOS ET AL.	
	<b>Examiner</b> Ileana Popa	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 21 February 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 24-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 24-28 is/are rejected.
- 7) ☒ Claim(s) 24 and 27 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
2. Claims 1-23 have been cancelled. Claim 24 has been amended.  
Claims 24-28 are pending and under examination.
3. All previously made rejections are hereby withdrawn. However, new grounds of rejection are made below.

Applicant states that, in the telephone interview that took place on 18 April 2007, both the Examiner and SPE Joseph Woitach indicated that the instant claims would be allowable if Applicant amended the claims to recite "organized bone formation" and submitted a declaration indicating that organized bone formation represents an unexpected result. Applicant also states that SPE Joseph Woitach indicated that such amendments would not necessitate further search and consideration. This is incorrect; during the interview, Applicant was informed that the newly amended claims require new considerations with respect to the prior art. Applicant was also informed that, even if the declaration for unexpected results would be considered, the claimed invention would still not be patentable over the newly identified prior art, which teaches organized bone formation by using mesenchymal cells transfected with a nucleic acid encoding for BMP-2 (see the interview summary).

***Claim Objections***

4. Claim 24 and 27 are objected to because of the recitation of "bone morphogenesis protein". Appropriate correction to "bone morphogenic protein" is required.

***Specification***

5. The disclosure is objected to because of the recitation of " bone morphpgetic proteins" on p. 1, line 12).

Appropriate correction to "bone morphogenic protein" is required.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruder et al. (J Cell Biochem, 1994, 56: 283-294), in view of Bonadio et al. (U.S. Patent No. 5,763,416, of record).

Bruder et al. teach the implanting autologous mesenchymal stem cells (MSCs) in combination with human BMP-2 to induce organized and functional bone formation in humans, wherein the MSCs are capable of responding to BMP-2 (i.e., MSCs express an

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endogenous BMP-2 receptor) (claims 24 and 27), and wherein the MSCs are isolated and expanded in culture or sub-cultured for 20 passages (claims 25 and 26) (p. 283, columns 1 and 2, p. 284, columns 1 and 2, p. 289, column 2, p. 290, columns 1 and 2, p. 291, column 2, p. 292, column 1). Bruder et al. do not teach transforming MSCs with a nucleic acid encoding BMP-2 (claim 24) nor do they teach parathyroid hormone (PTH) or parathyroid hormone receptor (PTHr) (claim 28). Bonadio et al. teach treating bone defects by implanting into a patient bone progenitor cells transformed with a nucleic acid encoding BMP-2 (claim 24) or with a combination of BMP-2 and PTH/PTHr (claim 28), wherein the bone progenitor cells are any or all of those cells that have the capacity to form or contribute to the formation of new bone tissue, such as cells localized within the bone (i.e., cells such as bone marrow MSCs) (Abstract, column 2, lines 38-67, column 3, lines 1-6, column 4, lines 32-55, column 5, lines 31-40, column 6, lines 38-48, column 8, lines 56-67, column 9, lines 1-17). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Bruder et al. by transforming their MSCs with the constructs of Bonadio et al., with a reasonable expectation of success. One of skill in the art would have been motivated to do so in order to make BMP-2 and PTH available for a longer period of time, since the art teaches that factors such as growth factors and hormones are instable and have a short half-life. One of skill in the art would have been expected to have a reasonable expectation of success in making and using such a composition because the art teaches that such compositions can be successfully made and used. With respect to the limitations of autocrine and paracrine effects (claim 24), since the implanted MSCs

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express BMP-2 receptor (see above), BMP-2 must necessarily exert both autocrine (on implanted transformed MSCs) and paracrine (on host MSCs) effects (claim 24). Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Since the above cited art teaches organized bone formation by using mesenchymal cells transfected with a nucleic acid encoding for BMP-2, Applicant's 1.132 Declaration filed on 02/21/2007 claiming unexpected results (i.e., organized bone formation) is not found persuasive.

8. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

/Joseph Woitach/  
Joseph Woitach  
SPE 1633